**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

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| In re Application of: | : | Barnea |
| Serial No: 10/670,490 | : | Group Art Unit: 1643 |
| Attorney Docket No: 120785.00311 | : | Confirmation No: 8761 |
| Filed: September 25, 2003 | : | Examiner: Canella, Karen A. |

For: ANTIPROLIFERATIVE AND ANTIVIRAL PROTEINS AND PEPTIDES

## AMENDMENT AND RESPONSE TO OFFICE ACTION

Mailstop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

This Amendment and Response is filed in response to the Office Action dated September 24, 2007. A request for a one-month extension of time is enclosed. Please charge any requisite fees relating to this amendment to Deposit Account No. 50-0436.

The following amendments and remarks are respectfully submitted for the Examiner's consideration.

## CLAIMS

This listing of the claims replaces any and all prior versions and listings of claims in the application:

Claims 1-8 (Canceled)

9. (Currently amended) A method of inhibiting the proliferation of cancer cells in a subject comprising administering, to the subject, an effective amount of at least one isolated peptide having a sequence selected from:

~~Cys Val His Ala Tyr Arg Ser (SEQ ID NO:1);~~
Cys Val His Ala Tyr Arg Ala (SEQ ID NO:2);
Cys Val His Ala Phe Arg Ser (SEQ ID NO:3); and
~~Cys Val His Ala Phe Arg Ala (SEQ ID NO:4);~~
~~Cys Val His Ser Tyr Arg Ser (SEQ ID NO:5);~~
~~Cys Val His Ser Tyr Arg Ala (SEQ ID NO:6);~~
~~Cys Val His Ser Phe Arg Ser (SEQ ID NO:7);~~
Cys Val His Ser Phe Arg Ala (SEQ ID NO:8);
~~Cys Val His Thr Tyr Arg Ser (SEQ ID NO:9);~~
~~Cys Val His Thr Tyr Arg Ala (SEQ ID NO:10);~~
~~Cys Val His Thr Phe Arg Ser (SEQ ID NO:11); and~~
~~Cys Val His Thr Phe Arg Ala (SEQ ID NO:12);~~

wherein the sequence ~~peptide~~ exhibits an antiproliferative activity.

10. (Original) The method of claim 9, where the cancer cells are breast cancer cells.

11. (Original) The method of claim 9, where the cancer cells are lung cancer cells.

12. (Original) The method of claim 9, where the cancer cells are colon cells.

13. (Original) The method of claim 9, where the cancer cells are melanoma cells.

14. (Original) The method of claim 9, where the cancer cells are leukemia cells.

15. (Currently amended) A method of inhibiting the proliferation of viral infection in a subject comprising administering, to the subject, an effective amount at least one isolated peptide having a sequence selected from:

~~Cys Val His Ala Tyr Arg Ser (SEQ ID NO:1);~~
Cys Val His Ala Tyr Arg Ala (SEQ ID NO:2);
Cys Val His Ala Phe Arg Ser (SEQ ID NO:3); and
~~Cys Val His Ala Phe Arg Ala (SEQ ID NO:4);~~
~~Cys Val His Ser Tyr Arg Ser (SEQ ID NO:5);~~
~~Cys Val His Ser Tyr Arg Ala (SEQ ID NO:6);~~
~~Cys Val His Ser Phe Arg Ser (SEQ ID NO:7);~~
Cys Val His Ser Phe Arg Ala (SEQ ID NO:8);
~~Cys Val His Thr Tyr Arg Ser (SEQ ID NO:9);~~
~~Cys Val His Thr Tyr Arg Ala (SEQ ID NO:10);~~
~~Cys Val His Thr Phe Arg Ser (SEQ ID NO:11); and~~
~~Cys Val His Thr Phe Arg Ala (SEQ ID NO:12);~~

wherein the sequence ~~peptide~~ exhibits an antiproliferative activity.

16. (Original) The method of claim 15, where the virus is human immunodeficiency virus type 1.

17. (Original) The method of claim 15, where the virus is a Bunyavirus.

18. (Original) The method of claim 15, where the virus is a Togavirus.

19. (Original) The method of claim 15, where the virus is a Reovirus.

20. (Original) The method of claim 15, where the virus is a Herpevirus.

21. (Original) The method of claim 15, where the virus is a Poxvirus.

22. (Previously presented) An isolated peptide selected from the group consisting of:
Cys Val His Ala Tyr Arg Ser (SEQ ID NO:1);

Cys Val His Ala Tyr Arg Ala (SEQ ID NO:2);

Cys Val His Ala Phe Arg Ser (SEQ ID NO:3);

Cys Val His Ala Phe Arg Ala (SEQ ID NO:4);

Cys Val His Ser Tyr Arg Ser (SEQ ID NO:5);

Cys Val His Ser Tyr Arg Ala (SEQ ID NO:6);

Cys Val His Ser Phe Arg Ser (SEQ ID NO:7);

Cys Val His Ser Phe Arg Ala (SEQ ID NO:8);

Cys Val His Thr Tyr Arg Ser (SEQ ID NO:9);

Cys Val His Thr Tyr Arg Ala (SEQ ID NO:10);

Cys Val His Thr Phe Arg Ser (SEQ ID NO:11); and

Cys Val His Thr Phe Arg Ala (SEQ ID NO:12).

23. (Canceled)

24. (Canceled)

25. (Currently amended) A composition comprising an excipient and at least one isolated peptide ~~having a sequence~~ consisting essentially of:

Cys Val His Ala Tyr Arg Ser (SEQ ID NO:1);

Cys Val His Ala Tyr Arg Ala (SEQ ID NO:2);

Cys Val His Ala Phe Arg Ser (SEQ ID NO:3);

Cys Val His Ala Phe Arg Ala (SEQ ID NO:4);

Cys Val His Ser Tyr Arg Ser (SEQ ID NO:5);

Cys Val His Ser Tyr Arg Ala (SEQ ID NO:6);

Cys Val His Ser Phe Arg Ser (SEQ ID NO:7);

Cys Val His Ser Phe Arg Ala (SEQ ID NO:8);

Cys Val His Thr Tyr Arg Ser (SEQ ID NO:9);

Cys Val His Thr Tyr Arg Ala (SEQ ID NO:10);

Cys Val His Thr Phe Arg Ser (SEQ ID NO:11); or

Cys Val His Thr Phe Arg Ala (SEQ ID NO:12).

26. (Currently amended) A method of inhibiting proliferation of cancer cells in a subject comprising administering to the subject an effective amount of at least one isolated peptide ~~having a sequence~~ consisting essentially of:

~~Cys Val His Ala Tyr Arg Ser (SEQ ID NO:1);~~
Cys Val His Ala Tyr Arg Ala (SEQ ID NO:2);
Cys Val His Ala Phe Arg Ser (SEQ ID NO:3); or
~~Cys Val His Ala Phe Arg Ala (SEQ ID NO:4);~~
~~Cys Val His Ser Tyr Arg Ser (SEQ ID NO:5);~~
~~Cys Val His Ser Tyr Arg Ala (SEQ ID NO:6);~~
~~Cys Val His Ser Phe Arg Ser (SEQ ID NO:7);~~
Cys Val His Ser Phe Arg Ala (SEQ ID NO:8);
~~Cys Val His Thr Tyr Arg Ser (SEQ ID NO:9);~~
~~Cys Val His Thr Tyr Arg Ala (SEQ ID NO:10);~~
~~Cys Val His Thr Phe Arg Ser (SEQ ID NO:11); and~~
~~Cys Val His Thr Phe Arg Ala (SEQ ID NO:12)~~.

27. (Currently amended) A method of inhibiting proliferation of viral infection in a subject comprising administering to the subject an effective amount of at least one isolated peptide ~~having a sequence~~ consisting essentially of:

~~Cys Val His Ala Tyr Arg Ser (SEQ ID NO:1);~~
Cys Val His Ala Tyr Arg Ala (SEQ ID NO:2);
Cys Val His Ala Phe Arg Ser (SEQ ID NO:3); or
~~Cys Val His Ala Phe Arg Ala (SEQ ID NO:4);~~
~~Cys Val His Ser Tyr Arg Ser (SEQ ID NO:5);~~
~~Cys Val His Ser Tyr Arg Ala (SEQ ID NO:6);~~
~~Cys Val His Ser Phe Arg Ser (SEQ ID NO:7);~~
Cys Val His Ser Phe Arg Ala (SEQ ID NO:8);
~~Cys Val His Thr Tyr Arg Ser (SEQ ID NO:9);~~
~~Cys Val His Thr Tyr Arg Ala (SEQ ID NO:10);~~
~~Cys Val His Thr Phe Arg Ser (SEQ ID NO:11); and~~

~~Cys Val His Thr Phe Arg Ala (SEQ ID NO:12)~~.

28. (Currently amended) An isolated peptide having a sequence selected from:

~~Cys Val His Ala Tyr Arg Ser (SEQ ID NO:1);~~

Cys Val His Ala Tyr Arg Ala (SEQ ID NO:2);

Cys Val His Ala Phe Arg Ser (SEQ ID NO:3); and

~~Cys Val His Ala Phe Arg Ala (SEQ ID NO:4);~~

~~Cys Val His Ser Tyr Arg Ser (SEQ ID NO:5);~~

~~Cys Val His Ser Tyr Arg Ala (SEQ ID NO:6);~~

~~Cys Val His Ser Phe Arg Ser (SEQ ID NO:7);~~

Cys Val His Ser Phe Arg Ala (SEQ ID NO:8);

~~Cys Val His Thr Tyr Arg Ser (SEQ ID NO:9);~~

~~Cys Val His Thr Tyr Arg Ala (SEQ ID NO:10);~~

~~Cys Val His Thr Phe Arg Ser (SEQ ID NO:11); and~~

~~Cys Val His Thr Phe Arg Ala (SEQ ID NO:12),~~

wherein the sequence ~~peptide~~ exhibits an antiproliferative activity.

29. (Currently amended) A composition comprising an excipient and at least one isolated peptide having a sequence selected from:

~~Cys Val His Ala Tyr Arg Ser (SEQ ID NO:1);~~

Cys Val His Ala Tyr Arg Ala (SEQ ID NO:2);

Cys Val His Ala Phe Arg Ser (SEQ ID NO:3); and

~~Cys Val His Ala Phe Arg Ala (SEQ ID NO:4);~~

~~Cys Val His Ser Tyr Arg Ser (SEQ ID NO:5);~~

~~Cys Val His Ser Tyr Arg Ala (SEQ ID NO:6);~~

~~Cys Val His Ser Phe Arg Ser (SEQ ID NO:7);~~

Cys Val His Ser Phe Arg Ala (SEQ ID NO:8);

~~Cys Val His Thr Tyr Arg Ser (SEQ ID NO:9);~~

~~Cys Val His Thr Tyr Arg Ala (SEQ ID NO:10);~~

~~Cys Val His Thr Phe Arg Ser (SEQ ID NO:11); and~~

~~Cys Val His Thr Phe Arg Ala (SEQ ID NO:12),~~

wherein the sequence ~~peptide~~ exhibits an antiproliferative activity.

30. (Previously presented) A composition consisting essentially of an isolated peptide selected from the group consisting of:

Cys Val His Ala Tyr Arg Ser (SEQ ID NO:1);
Cys Val His Ala Tyr Arg Ala (SEQ ID NO:2);
Cys Val His Ala Phe Arg Ser (SEQ ID NO:3);
Cys Val His Ala Phe Arg Ala (SEQ ID NO:4);
Cys Val His Ser Tyr Arg Ser (SEQ ID NO:5);
Cys Val His Ser Tyr Arg Ala (SEQ ID NO:6);
Cys Val His Ser Phe Arg Ser (SEQ ID NO:7);
Cys Val His Ser Phe Arg Ala (SEQ ID NO:8);
Cys Val His Thr Tyr Arg Ser (SEQ ID NO:9);
Cys Val His Thr Tyr Arg Ala (SEQ ID NO:10);
Cys Val His Thr Phe Arg Ser (SEQ ID NO:11); and
Cys Val His Thr Phe Arg Ala (SEQ ID NO:12).

## REMARKS

Applicants' attorney wishes to thank the Examiner for the careful attention given the present application. Claims 9-22 and 25-30 are pending. Claims 9, 15, and 25-29 are amended. Claims 1-8, 23 and 24 were previously canceled.

35 U.S.C. § 112, second paragraph: Indefiniteness

The Examiner has rejected claims 25-27 under 35 U.S.C. § 112, second paragraph as being indefinite. The Examiner states that "having a sequence consisting essentially of" is indefinite because "having" before "consisting essentially of" is midway between "consisting of" and "comprising." Applicant respectfully disagrees. The Examiner is incorrect that "having" is necessarily open language. As explained in the MPEP, "having" must be interpreted in light of the specification to determine if closed or open meaning is intended. See MPEP, 8th Ed., §2111.03 (Rev. No. 5); Lampi Corp. v. American Power Products Inc., 228 F.3d 1365, 1376 (Fed. Cir. 2000). Notwithstanding, solely to facilitate and expedite allowance of the present claims, Applicant has amended the claims to delete "having a sequence" as suggested by the Examiner. Applicants respectfully request that the rejection be withdrawn.

35 U.S.C. § 112, first paragraph: Written Description

The Examiner has rejected claims 9-21 and 25-29 as failing to comply with the written description requirement. The Examiner indicates that "having a sequence consisting essentially of" in claims 25-27 is broadly interpreted as "including." The Examiner recognizes that claims 9-21 and 26-29 recite that the peptide exhibits an antiproliferative activity, but argues that the specification fails to adequately describe a genus of proteins that exhibit antiproliferative

activity because the genus tolerates members which act by completely different mechanisms than those exerted by SEQ ID NOS:1-12. Applicant respectfully disagrees.

Notwithstanding, solely to facilitate and expedite allowance of the present claims, Applicant has amended Claims 9, 15 and 28-29 to recite that the sequence exhibits an antiproliferative activity. Claims 10-14 and 16-21 depend from claims 9 and 15, respectively. Applicant respectfully submits that the amended claims are allowable and request that the rejection be withdrawn.

Solely to facilitate and expedite allowance of the present claims, Applicant has amended Claims 25-27 to delete "having a sequence." The phrase "consisting essentially of" as recited in claims 25-27 is understood to limit the scope of a claim to the specified materials and any materials that do not materially affect the basic and novel characteristics of the claimed invention. See MPEP, 8th Ed., §2111.03 (Rev. No. 5); In re Herz, 537 F.2d 549 (CCPA 1976). Applicant respectfully submits that the amended claims are allowable and request that the rejection be withdrawn.

35 U.S.C. § 112, first paragraph: Enablement

The Examiner has rejected claims 9-22 and 25-30 under 35 U.S.C. §112, first paragraph as not enabled by the specification. The Examiner argues that only SEQ ID Nos. 2, 3 and 8 have antiproliferative activity. The Examiner argues that one of skill in the art would be subject to undue experimentation to carry out method claims 9-21, 26 and 27 or to use the products of claims 28 and 29 with peptides other than SEQ ID NOS: 2, 3 and 8. The Examiner argues that one of skill in the art would be subject to undue experimentation to use all of the peptides of claims 22, 25 and 30.

As a preliminary matter, the Examiner's burden is to show that the specification fails to teach how to make and use the claimed invention without undue experimentation, or that the scope of enablement is not commensurate with the scope of the claims. See MPEP, 8th Ed. §2164.04. Applicant respectfully submits that the Examiner has failed to meet that burden.

As discussed in the Response filed May 30, 2007, the peptides of the invention demonstrated varying levels of antiproliferative activity, as shown in Figure 9. One skilled in the art would have no difficulty determining, based on the specification and level of skill in the art, which peptides of the claims provide a desired level of antiproliferative activity. One skilled in the art would not require undue experimentation to make and use the invention. Further, methods of making the peptides is described, for example, in the specification on page 11, lines 22-28, and by methods well-known in the art. Methods of using the peptides is described, for example, in the specification on page 11, line 29 to page 12, line 12 and as known in the art. Thus, the specification fully enables one skilled in the art to both make and use the claimed invention. Accordingly, the Examiner has failed to meet her burden to show that the claims are not enabled. Notwithstanding, solely to facilitate and expedite allowance of the present claims, Applicant has amended the claims to recite only SEQ ID NOS: 2, 3 and 8, and respectfully requests that the rejection be withdrawn.

The Examiner further argues that the MCF7 assay fails to provide a nexus with a method of treatment of a subject having cancer or a viral infection; that the art teaches that compounds that show favorable activity *in vitro* may fail to show favorable activity in a clinical treatment; and that undue experimentation is required to determine a delivery means in quantities which would be efficacious including how to stabilize the peptides *in vivo* or how to target the peptides to the appropriate disease site.

First, Applicant respectfully submits that the standard of enablement does not require animal studies. As stated in the MPEP, "lack of working examples or lack of evidence that the claimed invention works as described should never be the sole reason for rejecting the claimed invention on the grounds of lack of enablement." MPEP 2164.02. The Examiner is required to provide evidence that the assay model does not correlate with a claimed method of use. See id. No such evidence has been provided. "[A] rigorous correlation is not necessary where the disclosure of pharmacological activity is reasonable based upon the probative evidence." Cross v. Iizuka, 753 F.2d 1040,1050 (Fed.Cir. 1985). Applicant submits that MCF7 cell assays provide merely a representative example and that the use of MCF7 assays is sufficient to reasonably demonstrate antiproliferative activity.

Second, Applicant respectfully submits that undue experimentation would not be required to determine a delivery means. Undue experimentation is determined on the basis of consideration of factors discussed in In re Wands, 858 F.2d 731, 737 (Fed.Cir. 1988). These include the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention based on the disclosure. Id. A "patent need not teach, and preferably omits, what is well known in the art." Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1384, (Fed.Cir. 1986).

Applicant submits that the use of peptides as therapeutic agents and a variety of peptide stabilization mechanisms were well known in the art prior to the present application. See, e.g., Torchilin, V.P. et al., Peptide and protein drug delivery to and into tumors: Challenges and solutions, Drug Discov. Today, 8:159-66 (2003)(Abstract) [Exhibit A]. The half life of a

peptide can be measured by routine experimentation and the mode and amount of administration adjusted accordingly, as appropriate to a given target molecule.

Applicant submits that it would be a matter of routine experimentation for one of ordinary skill in the art to test clinical activity of the claimed peptides and to determine an effective amount. Further, it would be a matter of routine experimentation for one of ordinary skill in the art to determine a means of delivery of the claimed peptides to a target site. "The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation." MPEP 2164.01. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

35 U.S.C. § 102(e)

The Examiner has withdrawn the rejection of claims 9-11, 14, 22 and 25 under 35 U.S.C. § 102(e) as anticipated by Barnea (U.S. Patent No. 5,648,340) ("Barnea"). Applicant thanks the Examiner for her careful consideration of the arguments.

## CONCLUSION

It is believed that the pending claims are in condition for allowance and notice to such effect is respectfully requested. The Commissioner is hereby authorized to charge deposit account No. 50-0436 for any additional fees that may be due in connection with this response.

Should the Examiner have any questions regarding this application, the Examiner is invited to initiate a telephone conference with the undersigned.

Respectfully submitted,

By: _____
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Dated: January 24, 2008

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